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Inventors: Anderson and Montelione  
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homologous to the determined three dimensional structure; and

- (E) correlating a biochemical function corresponding to the identified homologous structure to a biochemical function for the stable polypeptide domain.

#### REMARKS

Claims 1-14 and 17 are pending in the instant application. Claims 1-14 and 17 have been rejected. In response, the Applicants have amended claim 1 and canceled claims 2 and 17. No new matter has been added by these amendments. Reconsideration is respectfully requested in light of these amendments and the following remarks.

#### I. Rejection of Claims Under 35 U.S.C. § 102(b)

The rejection of claims 15 and 16 U.S.C. 102(b) as being anticipated by the University of Alabama at Birmingham campus has been deemed moot in view of the cancellation of claims 15 and 16.

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## II. Rejection of Claims Under 35 U.S.C. § 103(a)

The rejection of claims 1, 5, 6 and 11-14 under 35 U.S.C. § 103(a) as being unpatentable over Wallace, et al. (1996) in view of Holm, et al. (1995) has been maintained. The rejection of claims 1-6 and 11-14 under 35 U.S.C. § 103(a) as being unpatentable over Wallace, et al. (1996) in view of Holm, et al. (1995) and further in view of Farber, et al. (1992) has been maintained. The rejection of claims 1, 5-9 and 11-14 under 35 U.S.C. § 103(a) as being unpatentable over Wallace, et al. (1996) in view of Holm, et al. (1995) and further in view of Friedrichs (1994) has been maintained. The rejection of claims 1 and 5-14 under 35 U.S.C. § 103(a) as being unpatentable over Wallace, et al. (1996) in view of Holm, et al. (1995) and further in view of Friedrichs (1994) and further in view of Bagby et al. (1997) has been maintained. The rejection of claims 1-9, 11-14 and 17 under 35 U.S.C. § 103(a) as being unpatentable over Wallace, et al. (1996) in view of Holm, et al. (1995) and further in view of Farber, et al. (1992) and further in view of Friedrichs (1994) has been maintained.

MPEP § 2143 states that to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be

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some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art to modify the reference or combine the reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art references when combined must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination must both be found in the prior art, and not based on the applicant's disclosure. *In re Vaack*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Further, the mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art suggests the desirability of the combination. MPEP § 2143.01. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990).

Wallace, et al. (1996) teach the skilled artisan that databases of 3D templates may be used to identify a potential biological function of an unknown protein. However, Wallace, et al. do not teach the prestep of parsing a database to identify protein coding regions nor does this reference provide any motivation to predict exon boundaries in a nucleotide sequence to identify

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protein domains. Accordingly, the Applicants have amended claim 1 to include the prestep of parsing a target polynucleotide into at least one putative polypeptide domain. Thus, the primary reference fails to teach or suggest all the limitations as now claimed.

The secondary references cited under 35 U.S.C. 103(a) fail to overcome the deficiencies in the teachings of this primary reference.

The teachings of Holm, et al. (1995) is a commentary article wherein the DALI method is disclosed as useful for studying protein structure. Holm, et al. do not teach or suggest the prestep of parsing a database to identify protein coding regions.

Farber, et al. (1992) disclose a neural network and information theory for determination of coding regions of DNA sequences. Only the hindsight vision afforded by the claimed invention could provide motivation to consider Wallace et al., Holm et al. and Farber et al. Wallace, et al. and Holm, et al. are protein biochemistry articles directed at the analysis of protein structure and function. Contrary to the Examiner's suggestion, it would not have been obvious to the ordinary protein biochemist after reading these disclosures to take the additional step of

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predicting exon boundaries in a polynucleotide sequence to identify protein domains.

Friedrichs (1994) and Bagby, et al. (1997) teach NMR methodologies. These references do not teach or suggest the prestep of parsing a database to identify protein coding regions.

## II. Conclusion

The Applicant believes that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE."

Respectfully submitted,

*Jane Massey Licata*

Jane Massey Licata  
Registration No. 37,257

Date: February 18, 2003  
Licata & Tyrrell P.C.  
66 E. Main Street  
Marlton, New Jersey 08053  
(856) 810-1515

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 2 and 17 have been canceled without prejudice.

Claim 1 has been amended as follows:

1. (Four Times Amended) A high-throughput method for determining the biochemical function of a protein or polypeptide domain of unknown three dimensional structure and function comprising:

(A) parsing a target polynucleotide into at least one putative polypeptide domain;

~~(A)~~ (B) identifying a putative polypeptide domain consisting of 50 to 300 amino acids that properly folds into a stable polypeptide domain consisting of 50 to 300 amino acids;

(B) ~~(C)~~ determining three dimensional structure of the stable polypeptide domain;

(C) ~~(D)~~ comparing the determined three dimensional structure of the stable polypeptide domain to known three-dimensional structures in a protein data bank, wherein said comparison identifies known structures

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within said protein data bank that are homologous  
to the determined three dimensional structure; and  
(D) ~~(E)~~ correlating a biochemical function corresponding to  
the identified homologous structure to a  
biochemical function for the stable polypeptide  
domain.